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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,352	10/08/2003	Kyoji Ogoshi	3190-044	8311

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 08/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/681,352	OGOSHI, KYOJI	
	Examiner	Art Unit	
	Suzanne M. Noakes, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,11-14 and 19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11-14 and 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A - Seq. Alignment*.

DETAILED ACTION

Status of the Claims

1. The amendments to the claims filed under 35 U.S.C. 111(a) are acknowledged. Applicants have cancelled claims 7-10. Claims 1-6, 11-14 and 19-24 are pending.

Priority

2. Applicants were informed in the previous Office action that the benefit of priority is not and would not be granted for the instant application because the two foreign applications filed in Japan to which priority is being requested have not been filed. As such, the previous Office action considered prior art before the earliest effective filing date of March 26, 2002. It is noted Applicants have not filed any foreign priority claims or replied or even mentioned anything directed to the denial for the claim to foreign priority. Thus, for purposes of this Office action, the earliest effective filing date is still deemed to be March 26, 2002.

Withdrawal of Objections/Rejections

3. The following is a list of objections and rejections that are hereby withdrawn.

Objections to the Claims:

The objections recited in Sections 4-6 and 8, 10 and 11-15 are withdrawn due to the amendments to the claims.

Maintained Objections/Rejections

Claim Objections

4. Claims 2, 12, 14, 21 and 24 are dependent claims of evaluating methods for screening a "cancer treatment medicine" (see claim 1) and evaluating "anticancer treatments" or "cancer treatments" (see claim 11 and 13). Said claims recite the phrase "wherein cancer is analyzed by distinguishing stomach cancer from other cancers". However, the corresponding independent claims do not provide any methods steps for how such analysis of distinguishing cancer types is accomplished. Thus, the lack of method steps in claims 1, 11 and 13 addressing discrimination between cancer types makes claims 2 and 14 confusing. Similarly, claims 21 and 24 recite said phrase and depend on claims to a composition (see claims 19 and 23), wherein no clear indication of such analysis for discriminating cancer types is apparent.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description:

6. Claims 1-6, 11-14 and 19-24 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The details of the rejections are described in the previous Office action in Section 16-19.

Scope of Enablement:

7. Claims 1-10 are drawn to an evaluating method to determine effective cancer treatment medicines based on analyzing a genus of polymorphic HLA genes, DRB1*, DQB1* and DPB1* (herein referred as HLA class II polymorphic genes) which encode of polypeptides with at least one amino acid change at one of 38 amino acid positions for DQB1*, or at least one amino acid change at one of 42 amino acid positions of DRB1* or at least one amino acid change at one of 15 amino acid positions of DPB1*, and encoded polypeptides thereof, in patients cared for by treatments consisting of surgery by itself or surgery in combination with either chemotherapy or immunotherapy, and identifying a polymorphic variant that has a statistical significant relationship with at least one of the treatments, wherein the identified polymorphic variants are used to generate a genus of three-dimensional structures, which are ultimately use for *in silico* screening of compounds that upon interaction with the three-dimensional structure might have the potential of being a "cancer treatment medicine" and said candidate compound is identified by positively correlating successful cancer treatments with a reduction or lack of growth of cancer cells or tumors. The details of the rejection are recited in the previous Office action in Section 20.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior ad are such that the subject

> matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being obvious over Davies *et al.* (J. Clinical Oncology, vol. 19, pp. 1279-1287, 2001) in view of Lee *et al.* (Gastroenterology, vol. 111, pp. 426-432, 1996). The details of the rejection is recited in the previous Office action on pp. 23-25, Section A.

B. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being obvious over Davies *et al.* (J. Clinical Oncology, vol. 19, pp. 1279-1287, 2001) in view of Lee *et al.* (Gastroenterology, vol. 111, pp. 426-432, 1996), Toh *et al.* (Protein Engineering, vol. 11, pp. 1027-1032, 1998), and Gibbs *et al.* (Science. Vol. 287, pp. 1969-1973, 2000). The details of the rejection is recited in the previous Office action on pp. 25-27, Section B.

Response to Arguments

9. Applicant's arguments filed 05 May 2006 have been fully considered but they are not persuasive.

10. The examiner has maintained the objection that claims 2, 12, 14, 21 and 24, which are dependent claims of evaluating methods for screening a "cancer treatment medicine" (see claim 1) and evaluating "anticancer treatments" or "cancer treatments" (see claim 11 and 13), are confusing at best and lack a correlation step of how to

distinguish stomach cancer from any other type of cancer. The amendments to the claims do not clear this up, and the remarks by Applicants also are not of assistance. It is simply stated that the addition of steps f) and g) is sufficient to overcome the rejection. However, the examiner disagrees with this assessment, it is no clearer how stomach cancer is distinguished from other cancer types simply by "providing statistically significant relationships of steps a-f".

11. The examiner has maintained the rejection of claims 1-6, 11-14 and 19-24 for lacking written description. Applicant's arguments have been fully considered but they are not persuasive. Applicant's entire argument over the three written description rejections recited in Sections 16-19 of the previous Office action consists of since Applicant's have amended the independent claims 1, 11, 13, 19 and 22 to now recite specific amino acid positions for which variations are possible and which thus may prove significant, that this overcomes satisfies the written description requirement. Specifically, Applicants suggest that since they have amended said claims to recite the specific *possible* positions for variations in the HLA genes, and specifically identify 38 different amino acid positions for DQB1*, 42 amino acid positions of DRB1* or 15 amino acid positions of DPB1*, that this is sufficient.

The examiner disagrees with this position because the MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly

> conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the

MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, while Applicants have identified potential variation sites, the claims still lack Written Description because there is no correlation between the structure and function of each site. As noted in Section 7 of the previous Office action, multiple human variants of HLA class II exist in nature, more could be generated in the lab, and the claims are not limited to specific polymorphic variants because although Applicants have somewhat narrowed the scope of possible variants, there are still thousands or millions of variations because for instance, the identification of *at least one* position of the 38 recited for HLA DQB1 could be one, two, three, five, ten, twenty or all thirty-eight, or any combination thereof and thus is of no help whatsoever. Without identifying and sequencing each potential polypeptide, there is no way to know what their sequences are. Therefore, applicants have not disclosed, nor does the art recognize, the requisite structural and functional features of all the contemplated nucleic acid and amino acid sequence possibilities recited in the instant claims, which result in the disclosed statistical significant relationship with a cancer treatment, a feature deemed essential to the instant invention.

Furthermore, as stated in the previous Office action, the claims are also drawn to the three-dimensional structure of *each* of these possible variants where there is

absolutely no disclosure of a three-dimensional structure of any protein in the specification to support that Applicant's were in possession of even a single species out the thousands possible for *each* polypeptide encoded a an allelic variant with at least one, or more, changes in the recited positions. One way to obtain three-dimensional coordinates certainly is protein crystallography, NMR, or homology modeling, however, a known three-dimensional structure must be known for the later to be possible. The specification is again silent and only suggestive that this is possible, without actually demonstrating that Applicant's actually practiced or were in possession of this portion of their invention. At best, the specification simply indicates that one should run tests on a wide spectrum of **polymorphic alleles** in the hope that at least one of them can be isolated, crystallized or the structure solved by NMR or X-ray diffraction which would lead to a suitable screening three-dimensional model. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" (*Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

12. The examiner has maintained the scope of enablement rejection of claims 1-10 (now claims 1-6) as recited in the previous Office action in Section 20. Applicant's arguments have been fully considered but they are not persuasive. Applicant's argue that since they have changed their preamble from 'a screening method' to 'an evaluating method' and also recite specific positions of the specific genes at issue in conjunction with the amino acids encoded by the genes. This is not found persuasive because simply changing the preamble from screening to evaluating does and identifying the amino acids that potentially might be changed, does not negate the fact

that scope of the claims still exceed that which is described in the specification which would allow a skilled person to practice said invention without undue experimentation. Applicants have described a screening method that uses a homology model of an entire HLA heterodimer structure, however, they do not describe any other types of structures. By simply stating "a three –dimensional' structure provides for structures which were solved by both protein crystallography and protein NMR, both of which are non-trivial and unpredictable sciences and both which have not been described in the specification at all.

13. The examiner has maintained the 35 U.S.C. § 103(a) rejection of claims 1-6 (A. rejection) and 11-14 (B. rejection). Applicants assert that the rejections should be withdrawn because independent claims 1 and 11 now recite specific amino acid positions for which at least one position of HLA DQB1*, DRB1* and DPB1* are changed. However, this is not convincing because it still does not get over the prior art of record. Specifically, Lee et al. teach that HLA Class II genes are associated with several cancers (see line 1-2, 1st column, p.426). Namely, "HLA-DQB1*0301 is more common in Caucasian patients with gastric adenocarcinoma than noncancer controls" (see conclusions, p. 426). Thus, they identify a specific polymorphic variant of the HLA-DQB1* gene which is indicative of stomach cancer in Caucasian patients. A sequence alignment of the HLA-DQB1*0301 with that of HLA-DQB1*0402 shows that there are differences between these two alleles at amino acid positions 9, 45, 55, 56, 66, 67, 70, 71 and 74, all of which are amino acid positions recited in the claims. Since Applicants do not provide any sort of information in the specification or in the claims of a reference

sequence for which these amino acid changes are to be gauged, the sequence alignment (see attached, Appendix A) clearly shows that the Lee et al. reference does indeed provide information of changes at the positions indicated in the claims. Thus, the rejection and art of record still stands.

New Objections/Rejections

Claim Rejections - 35 USC § 112 – 2nd paragraph

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-6, 11-14 and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite an evaluating method to determine effective cancer treatment medicines by performing steps a-f and wherein for the HLA DQB1* gene in (a) –21, -6, -5, -4, 3, 9, 14 etc. However, for all of i), ii) and iii) HLA DQB1*, HLA DRB1* and HLA DPB1*, and the recited amino acid positions, the numbers suggest a reference point, a fixed starting and fixed ending point. Nonetheless, there is not necessarily any fixed starting or ending point for polymorphic variants, some may be variants by the sheer fact that they are shorter or longer. An examiner search of the NCBI nucleotide data base gave 1580 different deposited sequences for HLA DPB1 of varying lengths and sizes; since there is no disclosure in the specification as to the exact sequence to which these amino acids positions are directed, which of these 1580 publicly available

sequences is the reference sequence to which the examiner or a skilled artisan is to refer and to which the claims are directed?

Conclusion

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Noakes, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.30am to 4.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber (AU 1653) or Kathleen Kerr (AU 1656) can be reached on 571-272-0925 and 571-272-0931, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SMN
4 August 2006

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER

Sim

Appendix A

Click here to view these alignments graphically with the LALNVIEW program (mime-type *chemical/x-aln2*).

Click here to download LALNVIEW (Unix, Mac and PC versions available).
You can also have a look at a sample screen of LALNVIEW and access its documentation.

Results of SIM with:

Sequence 1: DQB1*0301, (229 residues)
Sequence 2: DQB1*0402, (229 residues)

using the parameters:

Comparison matrix: BLOSUM62
Number of alignments computed: 20
Gap open penalty: 12
Gap extension penalty: 4

Evaluate the significance of this protein sequence similarity score using PRSS at EMBnet-CH.

```
93.9% identity in 229 residues overlap; Score: 1142.0; Gap frequency: 0.0%

                        9   13           26                  45         55 56
DQB1*0301,       1 RDSPEDFVYQFKAMCYFTNGTERVRYVTRYIYNREEYARFDSDVEVYRAVTPLGPPDAEY
DQB1*0402,       1 RDSPEDFVFQFKGMCYFTNGTERVRGVTRYIYNREEYARFDSDVGVYRAVTPLGRLDAEY
                   ******** *** ************ ****************** *********  ****

                        66 67  70 71  74 75
DQB1*0301,      61 WNSQKEVLERTRAELDTVCRHNYQLELRTTLQRRVEPTVTISPSRTEALNHHNLLVCSVT
DQB1*0402,      61 WNSQKDILEEDRASVDTVCRHNYQLELRTTLQRRVEPTVTISPSRTEALNHHNLLVCSVT
                   *****  **  **  *********************************************

                                                                 167
DQB1*0301,     121 DFYPAQIKVRWFRNDQEETTGVVSTPLIRNGDWTFQILVMLEMTPQHGDVYTCHVEHPSL
DQB1*0402,     121 DFYPAQIKVRWFRNDQEETTGVVSTPLIRNGDWTFQILVMLEMTPQRGDVYTCHVEHPSL
                   ********************************************** *************

                       185
DQB1*0301,     181 QNPITVEWRAQSESAQSKMLSGIGGFVLGLIFLGLGLIIHHRSQKGLLH
DQB1*0402,     181 QNPIIVEWRAQSESAQSKMLSGIGGFVLGLIFLGLGLIIHHRSQKGLLH
                   **** ********************************************
```

41.7% identity in 12 residues overlap; Score: 25.0; Gap frequency: 0.0%

```
DQB1*0301,    131 WFRNDQEETTGV
DQB1*0402,     16 YFTNGTERVRGV
                   * *  *   **
```

22.7% identity in 22 residues overlap; Score: 22.0; Gap frequency: 0.0%

```
DQB1*0301,     30 YIYNREEYARFDSDVEVYRAVT
DQB1*0402,      7 FVFQFKGMCYFTNGTERVRGVT
                          *    *  * **
```

50.0% identity in 6 residues overlap; Score: 22.0; Gap frequency: 0.0%

```
DQB1*0301,     61 WNSQKE
DQB1*0402,    188 WRAQSE
                  *  * *
```

26.9% identity in 26 residues overlap; Score: 21.0; Gap frequency: 0.0%

```
DQB1*0301,     27 VTRYIYNREEYARFDSDVEVYRAVTP
DQB1*0402,     78 VCRHNYQLELRTTLQRRVEPTVTISP
                  * *  *  *        **      *
```

30.8% identity in 13 residues overlap; Score: 20.0; Gap frequency: 0.0%

```
DQB1*0301,      6 DFVYQFKAMCYFT
DQB1*0402,    152 DWTFQILVMLEMT
                  *   *   *   *
```

38.5% identity in 13 residues overlap; Score: 20.0; Gap frequency: 0.0%

```
DQB1*0301,    152 DWTFQILVMLEMT
DQB1*0402,      6 DFVFQFKGMCYFT
                  *  **   *   *
```

33.3% identity in 6 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,    188 WRAQSE
DQB1*0402,     61 WNSQKD
                  *  *
```

21.1% identity in 38 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,      7 FVYQFKAMCYFTNGTERVRYVTRYIYNREEYARFDSDV
DQB1*0402,     30 YIYNREEYARFDSDVGVYRAVTPLGRLDAEYWNSQKDI
                    *       *       * **       **     *
```

21.1% identity in 19 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,     59 EYWNSQKEVLERTRAELDT
DQB1*0402,    176 EHPSLQNPIIVEWRAQSES
                  *    *       **
```

33.3% identity in 9 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,    167 HGDVYTCHV
DQB1*0402,    111 HHNLLVCSV
                  *     * *
```

66.7% identity in 6 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,    223 SQKGLL
DQB1*0402,     63 SQKDIL
                  ***  *
```

36.4% identity in 11 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,     16 YFTNGTERVRY
DQB1*0402,     30 YIYNREEYARF
                  *  *  *  *
```

22.2% identity in 18 residues overlap; Score: 19.0; Gap frequency: 0.0%

```
DQB1*0301,    184 ITVEWRAQSESAQSKMLS
DQB1*0402,    127 IKVRWFRNDQEETTGVVS
                  * * *           *
```

26.3% identity in 19 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,    126 QIKVRWFRNDQEETTGVVS
DQB1*0402,     84 QLELRTTLQRRVEPTVTIS
                  *   *       * *   *
```

26.3% identity in 19 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,     84 QLELRTTLQRRVEPTVTIS
DQB1*0402,    126 QIKVRWFRNDQEETTGVVS
                  *   *       * *   *
```

25.0% identity in 12 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,    101 ISPSRTEALNHH
DQB1*0402,    163 MTPQRGDVYTCH
                    * *      *
```

100.0% identity in 4 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,    215 LGLI
DQB1*0402,    208 LGLI
                  ****
```

31.6% identity in 19 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,    176 EHPSLQNPITVEWRAQSES
DQB1*0402,     59 EYWNSQKDILEEDRASVDT
                  *    *  *  * **
```

100.0% identity in 4 residues overlap; Score: 18.0; Gap frequency: 0.0%

```
DQB1*0301,    208 LGLI
DQB1*0402,    215 LGLI
                  ****
```
